

CLAIMS

What is claimed:

- 5 1. A method of treating a subject suffering from anemia comprising administering a therapeutically effective amount of a TNF α antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNF α with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s $^{-1}$ or less, both determined by surface plasmon resonance, and neutralizes human TNF α cytotoxicity in a standard *in*
10 *vitro* L929 assay with an IC $_{50}$ of 1×10^{-7} M or less, such that the anemia is treated.
2. A method of treating a subject suffering from anemia comprising administering a therapeutically effective amount a TNF α antibody, or an antigen-binding fragment thereof, with the following characteristics:
- 15 a) dissociates from human TNF α with a K_{off} rate constant of 1×10^{-3} s $^{-1}$ or less, as determined by surface plasmon resonance;
- b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6,
20 7, 8 and/or 9;
- c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.
- 25 3. A method of treating a subject suffering from anemia comprising administering a therapeutically effective amount a TNF α antibody, or an antigen-binding fragment thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:1 and a heavy chain variable region (HCVR) comprising the amino acid
30 sequence of SEQ ID NO:2.

4. The method of any one of claims 1, 2, and 3, wherein the antibody, or antigen-binding fragment thereof, is D2E7.

5. The method of any one of claims 1, 2, and 3, wherein anemia is selected from the group consisting of: anemia related to rheumatoid arthritis, anemia of infection and chronic inflammatory diseases, iron deficiency anemia, autoimmune hemolytic anemia, myelophthisic anemia, aplastic anemia, hypoplastic anemia, pure red cell aplasia, anemia associated with renal failure or endocrine disorders, megaloblastic anemias, defects in heme or globin synthesis, sickle-cell anemia, sideroblastic anemia, anemia associated with chronic infections, and myelophthisic anemias.

6. A method for inhibiting human $\text{TNF}\alpha$ activity in a human subject suffering from anemia comprising administering a therapeutically effective amount of a $\text{TNF}\alpha$ antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human $\text{TNF}\alpha$ with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, both determined by surface plasmon resonance, and neutralizes human $\text{TNF}\alpha$ cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.

7. The method of claim 6, wherein anemia is selected from the group consisting of : anemia related to rheumatoid arthritis, anemia of infection and chronic inflammatory diseases, iron deficiency anemia, autoimmune hemolytic anemia, myelophthisic anemia, aplastic anemia, hypoplastic anemia, pure red cell aplasia, anemia associated with renal failure or endocrine disorders, megaloblastic anemias, defects in heme or globin synthesis, sickle-cell anemia, sideroblastic anemia, anemia associated with chronic infections, and myelophthisic anemias.

8. The method of any one of claims 6 and 7, wherein the $\text{TNF}\alpha$ antibody, or antigen-binding fragment thereof, is D2E7.

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9. A method of treating a subject suffering from anemia comprising administering a therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, to the subject, such that anemia is treated.

5 10. The method of claim 9, wherein anemia is selected from the group consisting of: anemia related to rheumatoid arthritis, anemia of infection and chronic inflammatory diseases, iron deficiency anemia, autoimmune hemolytic anemia, myelophthisic anemia, aplastic anemia, hypoplastic anemia, pure red cell aplasia, anemia associated with renal failure or endocrine disorders, megaloblastic anemias, defects in heme or globin
10 synthesis, sickle-cell anemia, sideroblastic anemia, anemia associated with chronic infections, and myelophthisic anemias.

11. A method of treating a subject suffering from anemia comprising administering a
15 therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, and at least one additional therapeutic agent to the subject, such that anemia is treated.

12. A kit comprising:
a) a pharmaceutical composition comprising a $\text{TNF}\alpha$ antibody, or an antigen
20 binding portion thereof, and a pharmaceutically acceptable carrier; and
b) instructions for administering to a subject the $\text{TNF}\alpha$ antibody pharmaceutical composition for treating a subject who is suffering from anemia.

13. A kit according to claim 12, wherein the $\text{TNF}\alpha$ antibody, or an antigen binding
25 portion thereof, is D2E7.